

What is the significance of abnormal liver function tests in people living with HIV infection?

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Background

- Combination antiretroviral therapy has resulted in a reduction in AIDS-related deaths and an ageing population¹. Management of medical co-morbidities has therefore become a central component of HIV care.
- Deaths due to liver disease in the general UK population are rising with a 400% increase in the standardised mortality rate reported between 1970 and 2010².
- Liver function tests are readily available biochemical laboratory tests commonly used to exclude liver disease and monitor chronic disease and adverse effects of drugs on the liver.
- 30% of requests for liver function tests by General Practitioners to University Hospitals Birmingham NHS Foundation Trust in 2016 contained at least one abnormal result³.
- An audit of the local guideline for the management of abnormal liver function tests was performed in order to explore the prevalence and common causes of abnormal liver function tests in persons living with HIV infection.

Methods

- Standard liver panels vary across clinical settings but local guidance recommends inclusion of alanine transferase (ALT) in routine blood monitoring of persons living with HIV infection to screen for liver injury. The cause of abnormal ALT is then investigated with liver aetiology screen including aspartate transferase (AST), gamma-glutamyltransferase (GGT), autoimmune liver disease profile (anti-nuclear antibody and anti-smooth muscle antibody), viral hepatitis screen (hepatitis B and C), body mass index (BMI), and ultrasound scan.
- The local guideline for management of abnormal liver function tests in persons living with HIV infection was audited in order to explore the prevalence and common causes of abnormal liver function tests.
- Data was retrospectively gathered on all registered persons living with HIV-1 infection with an abnormal ALT and/or AST and/or GGT between 1st January 2014 and 30th November 2017.

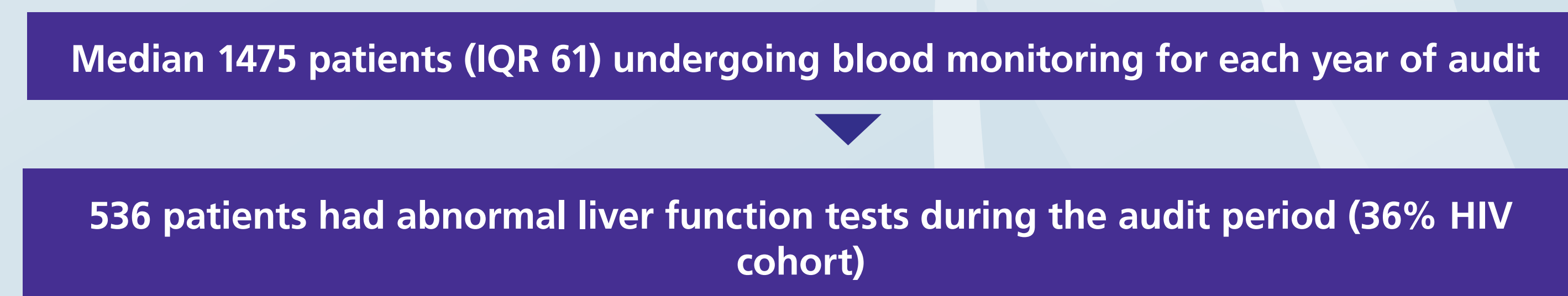
Results Table 1: Audit results



Investigation of abnormal liver function tests	Number	%
Liver immune profile	321 / 536	59.9
Hepatitis B surface antigen/Hepatitis C antibody	536 / 536	100.0
Ultrasound scan	286 / 536	53.4
Recorded BMI	531 / 536	99.1
Complete liver screen*	241 / 536	45.0

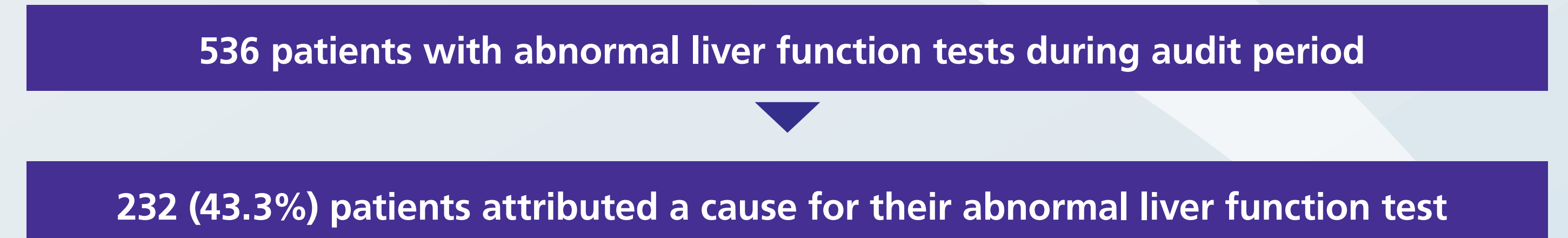
*Liver immune profile, viral hepatitis screen, USS and BMI result all available

Results Table 2: Characteristics of abnormal liver function tests



Characteristic	Number of patients	%
Recorded abnormal LFT prior to audit start date	294 / 536	54.9
Patient on combination antiretroviral therapy	345 / 536	64.4
VL <50 copies/mL	292 / 345	84.6
Pattern of abnormal liver function tests		
Hepatitis (abnormal ALT +/- AST)	153 / 536	28.5
Mixed pattern (abnormal ALT +/- AST and GGT)	227 / 536	42.4
Abnormal GGT	156 / 536	29.1
Abnormal ALT	318 / 536	59.3
Grade 1 ($\leq 3 \times$ upper limit normal (ULN))	289 / 318	90.9
Grade 2 ($>3 - \leq 5 \times$ ULN)	14 / 318	4.4
Grade 3 ($>5 - \leq 10 \times$ ULN)	9 / 318	2.8
Grade 4 ($>5 - \leq 10 \times$ ULN)	6 / 318	1.9

Results Table 3: Cause of abnormal liver function tests



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    A[536 patients with abnormal liver function tests during audit period] --> B[232 (43.3%) patients attributed a cause for their abnormal liver function test]
  
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Attributed cause	Number	%
Non-alcoholic fatty liver disease	85 / 232	36.6
Viral hepatitis	64 / 232	27.6
Excessive alcohol consumption	49 / 232	21.1
Antiretroviral medications*	13 / 232	5.6
Drugs (medication/recreational drug use)	8 / 232	3.4
Cancer	3 / 232	1.3
Acute infection ^{&}	3 / 232	1.3
Non-cirrhotic portal hypertension	2 / 232	0.9
Cardiopulmonary disease	2 / 232	0.9
Autoimmune hepatitis	1 / 232	0.4
Genetic haemochromatosis	1 / 232	0.4
Trauma	1 / 232	0.4

*Efavirenz, Rilpivirine, Nevirapine, Darunavir/r, Old NRTIs. &Primary syphilis, infective exacerbation COPD, acute viral illness

Audit Summary

- 36% of patients undergoing routine blood monitoring had abnormal liver function tests.
- 55% of liver aetiology screens performed were incomplete.
- Most patients had modifiable risk factors for liver injury on retrospective review of the electronic patient record.

Audit Limitations

- Duration for completion of liver aetiology screen was not stipulated and tests were often completed over many clinic attendances.
- Clinical diagnosis is often informed by the result of the liver aetiology screen which was not available for the majority of patients included in this audit.
- Patients often have multiple overlapping risk factors for liver injury and it is often difficult to determine the main driver of liver disease.

Audit Recommendations

1. All abnormal liver function tests should be investigated regardless of severity or duration.
2. All patients should undergo prospective review of known risk factors for liver disease in addition to screening with liver function tests at each clinic attendance.

Conclusion

- Adherence to local protocol for the management of abnormal liver function tests was poor however a significant and modifiable cause was identified in the majority of patients who did undergo investigation despite most patients having low-grade abnormalities.

References

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3. Newsome PN, Cramb R, Davison SM et al. Guidelines on the management of abnormal liver blood tests. *Gut* 2018;67(6):6-19.